REMARKS

Amendments to the Claims

Currently, claims 1, 3-17, and 19-21 are pending. Applicants have amended claim 1 to recite that the pharmaceutical compound is acid labile to distinguish the claimed invention from the prior art. Support for this amendment can be found on page 3, lines 29-30 and page 4, lines 1-5, 25-31. Accordingly, Applicants have cancelled claims 2 and 18 which became redundant. Also, in view of the amendment to claim 1, claims 3 and 19 have been amended to depend on claims 1 and 17.

Rejection of Claims 1, 5, 6, and 17 Under 35 U.S.C. §102 (b)

The Office Action rejects claims 1, 5, 6, and 17 under 35 U.S.C. §102(b) as being anticipated by Kouchiwa et al. (EP 0 264 259). Applicants respectfully traverse this rejection.

Claim 1 has been amended to recite that the pharmaceutical compound is acid labile. Kouchiwa et al. do not disclose or such at least one acid labile pharmaceutical compound. Therefore, because Kouchiwa et al. do not disclose or suggest each and every element of the claimed invention, this reference cannot anticipate the claimed invention and this rejection should be withdrawn.

Rejection of Claims 1-11 Under 35 U.S.C. §103(a)

The Office Action rejects claims 1-21 under 35 U.S.C. §103(a) as being obvious over GB 747,293 (hereinafter "the '293 patent") in view of Chen et al. (U.S. Pat. No. 6,544 556 B1) (hereinafter "Chen et al."). The Office Action also rejects claims 1-21 under 35 U.S.C. §103(a) as being obvious and over Phillips (U.S. Pat. No. 5,840,737) (hereinafter "Phillips") in view of the '293 patent and further in view of Chen et al. Applicants respectfully traverse the rejection.

a) Rejection over the '293 patent in view of Chen et al.

The Examiner states that the '293 patent teaches a pharmaceutical composition comprising a therapeutically effective amount of an acid-labile compound (erythromycin) in combination with acid neutralizers and buffers (See, Office Action, page 4). According to the Examiner, the '293 discloses as suitable physiologically acceptable acid neutralizers the following: aluminum hydroxide, calcium hydroxide, sodium acetate, magnesium trisilicate, sodium phosphate, calcium carbonate, sodium bicarbonate and sodium carbonate (Column 2, lines 78-85). The acid neutralizers (buffers) may be used alone or in suitable combinations (Column 3, lines 4-6). The Examiner further states that the composition disclosed in the '293 patents provides for adequate blood levels, whereby pH levels are effectively maintained. The Examiner admits that the '293 patent does not teach "solid" formulations.

With respect to Chen et al., the Examiner states that this reference teaches pharmaceutical formulations comprising a non-steroidal anti-inflammatory drug (hereinafter "NSAID") and a proton pump inhibitor in an amount effective to inhibit gastrointestinal side effects (See, Office Action, page 4). According to the Examiner, the pharmaceutical compositions are preferably administered as oral dosage forms.

The Examiner concludes that it would have been obvious to one of ordinary skill in the art (hereinafter referred to as a "skilled artisan") at the time the invention was made to incorporate oral, solid dosage forms, such as taught by Chen et al. within the liquid formulations of the '293 patent. The Examiner finds the motivation to do so because Chen et al. teach that oral dosage forms comprising proton pump inhibitors can be administered in effective and preferable dosage forms that include solid oral forms, such as tablets, granules or the like, or alternatively, in liquid oral forms. The Examiner states that the expected result would be improved, convenient solid dosage forms for the effective treatment of gastrointestinal disorders and conditions. Applicants

respectfully traverse the rejection.

The inventive concept of the present invention is that a solid pharmaceutical composition comprising a pharmaceutically acceptable protectant comprising a combination of a water-soluble acid neutralizer and a water-insoluble acid neutralizer exhibits superior protective qualities when administered to a patient in need of treatment thereof. The reason for this is that the combination of a water-soluble acid neutralizer and a water-insoluble acid neutralizer has been found to (a) increase pH levels in an acidic environment (such as the stomach) to a greater extent when compared to the use of either of these acid neutralizers alone; and (b) maintain the elevated pH levels for a greater time period in said acidic environment when compared to the use of either of these acid neutralizers alone (See, specification, page 5, lines 8-11). Increasing the pH levels in an acidic environment: (a) is comforting to the patient receiving said treatment; and (b) protects an acid-labile pharmaceutical compound from substantial degradation as it passes through the stomach (an acidic environment) to the upper intestinal tract.

The '293 patent discloses an oral suspension composition containing erythromycin, a buffer and a suspending agent. The buffer may be any acid neutralizing base or salt of a strong base or salt of a strong base and a weak acid. While the specification of the '293 patent states that "we may use any of the buffers alone or we may use a suitable combination of buffers," nowhere does the '293 patent disclose, suggest or teach the importance of a <u>combination</u> of a <u>water-soluble</u> acid neutralizer <u>and</u> a <u>water-insoluble</u> acid neutralizer. Even if a skilled artisan practicing the '293 patent selected a water-soluble acid neutralizer and a water-insoluble acid neutralizer, such a selection would be completely serendipitous. The Examiner argues that:

> "it is not necessary that the art recognize each and every benefit that accrues from these teachings, since the ingredients are incorporated for their intended purposes.

> The ingredients employed in the prior art are the same as those instantly employed by Applicants and therefore, it is expected that similar, beneficial results could be obtained using the ingredients of the art" (See, Office Action, page 11).

While true that the art does not have to recognize each and every benefit that accrues from it, Applicants submit that that because the art does not disclose, suggest or teach the importance of a combination of a water-soluble acid neutralizer and a water-insoluble acid neutralizer, it would not have been obvious to a skilled artisan to select this specific combination (out of the many possible acid neutralizers or combinations thereof taught by the '293 patent) and incorporate this combination with oral solid dosage forms taught by Chen et al. The innovative aspect of the present invention is the combination of a water-soluble acid neutralizer and a water-insoluble acid neutralizer, and nothing in the '293 patent discloses, suggests or teaches the importance of this combination.

Chen et al. do not cure this deficiency. Like the '293 patent, this reference is silent about the importance of the combination of a water-soluble acid neutralizer and a water-insoluble acid neutralizer. Chen et al. teach a solid oral dosage form comprising a NSAID and an enterically-coated proton pump inhibitor. Not only does Chen et al. not disclose the combination of a water-soluble acid neutralizer and a water-insoluble acid neutralizer, it employs an altogether different method to protect a proton pump inhibitor, namely, an enteric coating. The specification of the present invention states that it is preferable that the claimed formulations or pharmaceutical compounds included in the formulations not be enterically coated (See, the specification, page 4, lines 5-6).

Accordingly, neither the '293 patent nor Chen et al. alone or in combination, render the claimed invention obvious. To an artisan familiar with both the '293 and Chen et al., it would not have been obvious to arrive at the solid pharmaceutical formulations comprising a combination of a water-soluble acid neutralizer and a water-insoluble acid neutralizer since neither the '293

patent nor Chen et al. discloses the importance of the combination. There is nothing in the references to motivate the artisan to combine a water-soluble acid neutralizer and water-insoluble acid neutralizer. Just because the '293 patent discloses a wide variety of acid neutralizers, including both water-soluble and water-insoluble ones, it does not follow that the this patent teaches the importance of a combination of a water-soluble acid neutralizer and a water-insoluble acid neutralizer.

b) Rejection over Phillips in view of the '293 patent and in view of Chen et al.

The Examiner states that Phillips teaches a pharmaceutical composition and methods for treating and/or preventing gastrointestinal conditions comprising active ingredients of acid-labile compounds (for example, omeprazole, lansoprazole and derivatives thereof) and a bicarbonate salt of a Group IA metal, preferably sodium bicarbonate (See, Office Action, page 5). The Examiner further states that the composition is used for the treatment of gastrointestinal conditions. The Examiner states that Phillips teaches a water-soluble acid neutralizer, namely, sodium bicarbonate. The Examiner admits that Phillips does not teach a water-insoluble neutralizer.

The Examiner again describes the '293 reference as teaching a pharmaceutical composition which comprises both water-soluble and water-insoluble acid neutralizers or buffers, and states that it would have been obvious to incorporate the acid neutralizers taught by the '293 reference into the acid-labile formulation of Phillips. The Examiner also again describes Chen et al. as teaching pharmaceutical formulations comprising an NSAID and a proton pump inhibitor. The Examiner states that it would have been obvious to incorporate oral, solid dosage forms as taught by Chen et al. within the liquid formulations of either Phillips or the '293 patent. The Examiner finds the motivation in the fact that Chen et al. teach oral dosage forms which can be administered in effective

and preferable dosage as either solid or liquid forms to provide for the treatment of gastrointestinal side effects. Applicants respectfully traverse this rejection.

As discussed previously herein, the '293 patent does not teach the importance of the combination of a water-soluble acid neutralizer and a water-insoluble acid neutralizer. Therefore, it would not have been obvious to a skilled artisan to specifically incorporate a combination of a water-soluble acid neutralizer and a water-insoluble acid neutralizer selected from the neutralizers taught in the '293 patent into the acid- labile formulation of Phillips. A skilled artisan would simply not recognize the importance of selecting just any combination of acid neutralizers, but rather a specific combination of both a water-soluble acid neutralizer and a water-insoluble acid neutralizer. There is nothing in either of the '293 patent or Phillips that discloses, suggests or teaches the importance of this combination. Moreover, as the Examiner admits, Phillips teaches a specific acid neutralizer, namely, sodium bicarbonate. There is nothing in Phillips that suggests, motivates or teaches a skilled artisan to replace this specific acid neutralizer with a combination of a water-soluble acid neutralizer and a water-insoluble acid neutralizer. Indeed, Phillips specifically states that its disclosed combination of an NSAID and sodium bicarbonate is superior to the prior art compositions as it can be administered orally, in a single dose, and in lesser amounts than the prior art compositions (See, Phillips, column 9, line 65 through column 10, line 14). Therefore, there is absolutely nothing in Phillips that would motivate a skilled artisan to tamper with or alter the specifically disclosed acid neutralizer disclosed in Phillips and to replace it with combinations of other acid neutralizers, specifically a combination of a water-soluble acid neutralizer and a water-insoluble acid neutralizer.

Similarly, as Applicants have explained above, Chen et al. are silent about the importance of a combination of a water-soluble acid neutralizer and a water-insoluble acid neutralizer. Chen et al. teach a solid oral dosage form comprising a NSAID and an enterically-coated proton pump inhibitor. Not only does Chen et

al. not disclose the combination of a water-soluble acid neutralizer and a water-insoluble acid neutralizer, it employs an altogether different method to protect a proton pump inhibitor, namely, an enteric coating. In contrast, the specification of the present invention states that it is preferable that the claimed formulations or pharmaceutical compounds included in the formulations not be enterically coated (See, specification, page 4, lines 5-6).

Therefore, contrary to the Examiner's argument, a skilled artisan would not have been motivated to incorporate the dosage forms of Chen et al. within the liquid formulations of Phillips. Chen et al. teach an NSAID and a proton pump inhibitor covered with an enteric coating while Phillips teaches an aqueous solution/suspension comprising omeprazole or other substituted benzimidazoles and derivatives thereof and a bicarbonate salt of a Group IA metal, preferably, sodium bicarbonate. Even if one were to combine the Phillips and Chen et al., for which Applicants submit there is not motivation, suggestion or teaching to do so, the resulting formulation would still not comprise a combination of a water-soluble acid neutralizer and a water-insoluble acid neutralizer. Neither Chen et al. nor Phillips disclose, suggest or teach such combination; specifically Chen et al. teach enteric coatings and Phillips teaches a bicarbonate salt of a Group IA metal.

Therefore, Applicants respectfully submit that the rejection of claims 1-11 under 35 U.S.C. §103 are improper and should be withdrawn.

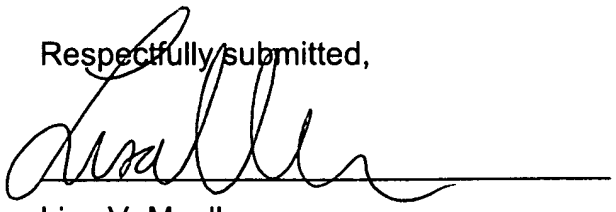
CONCLUSION

Applicants respectfully submit that the claims comply with the requirements of 35 U.S.C. Sections 102 and 103. Accordingly, a Notice of Allowance is believed in order and is respectfully requested.

Should the Examiner have any questions concerning the above, the Examiner is respectfully requested to contact the undersigned at the telephone number listed below. If the Examiner notes any matters which the Examiner

believes may be expedited by a telephone interview, the Examiner is requested to contact the undersigned.

Respectfully submitted,



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